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FILE 'HOME' ENTERED AT 13:59:40 ON 22 APR 2003

=> fil reg

=> s cholrin
             0 CHOLRIN
L1           0 CHOLRIN

=> s chlorin
L2         455 CHLORIN

=> fil hcapl

=> s l2
L3       38921 L2

=> s pDT or photodynamic therapy
          2377 PDT
            23 PDTS
          2392 PDT
                 (PDT OR PDTS)
         10534 PHOTODYNAMIC
           323 PHOTODYNAMICS
         10771 PHOTODYNAMIC
                 (PHOTODYNAMIC OR PHOTODYNAMICS)
        192215 THERAPY
         11958 THERAPIES
        198683 THERAPY
                 (THERAPY OR THERAPIES)
          4649 PHOTODYNAMIC THERAPY
                 (PHOTODYNAMIC(W)THERAPY)
L4        5162 PDT OR PHOTODYNAMIC THERAPY

=> s l3 and l4
L5         434 L3 AND L4

=> s restenosis or intimal hyperplasia
          4546 RESTENOSIS
          3723 INTIMAL
         20121 HYPERPLASIA
           718 HYPERPLASIAS
         20450 HYPERPLASIA
                 (HYPERPLASIA OR HYPERPLASIAS)
           734 INTIMAL HYPERPLASIA
                 (INTIMAL(W)HYPERPLASIA)
L6        5058 RESTENOSIS OR INTIMAL HYPERPLASIA

=> s l5 and l6
L7           1 L5 AND L6

=> d

L7   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2003 ACS
AN   2002:742747  HCAPLUS
DN   138:100254
TI   Photodynamic therapy: pharmacological aspects,
     applications and recent advances in drug development
AU   Simplicio, Fernanda Ibanez; Maionchi, Florangela; Hioka, Noboru
CS   Departamento de Quimica, Universidade Estadual de Maringa, Maringa, PR,
     87020-900, Brazil
SO   Quimica Nova (2002), 25(5), 801-807
     CODEN: QUNODK; ISSN: 0100-4042
PB   Sociedade Brasileira de Quimica
DT   Journal; General Review
LA   Portuguese
RE.CNT  37    THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> s l3 and l5
L8         434 L3 AND L5

=> s l3 and l6
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L9 11 L3 AND L6

=> d tot all

L9 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:742747 HCAPLUS
DN 138:100254
TI Photodynamic therapy: pharmacological aspects, applications and recent advances in drug development
AU Simplicio, Fernanda Ibanez; Maionchi, Florangela; Hioka, Noboru
CS Departamento de Quimica, Universidade Estadual de Maringa, Maringa, PR, 87020-900, Brazil
SO Quimica Nova (2002), 25(5), 801-807
CODEN: QUNODK; ISSN: 0100-4042
PB Sociedade Brasileira de Quimica
DT Journal; General Review
LA Portuguese
CC 1-0 (Pharmacology)
Section cross-reference(s): 8
AB A review. Photodynamic therapy (PDT) is a clin. procedure using photosensitive drug compds. and light and is characterized by good efficiency, less traumatic effects, low recovery time, and few side-effects. This modality of treatment can be used for cancer, aged-related macular degeneration (AMD), psoriasis, arthritis, arterial **restenosis**, and other disorders. The first approved drug for PDT use by the US Food and Drug Administration is Photofrin used in cancer treatment, followed by Levulan Kerastick. A new generation PDT drug Visudyne (BPDMA) has been recently approved for AMD treatment. A concise history of PDT, tech. information, and some addnl. drugs under development are also discussed.
ST review photodynamic therapy pharmacol drug development advance
IT Drug design
Photodynamic therapy
(photodynamic therapy pharmacol. aspects, applications and recent advances in drug development)
IT 5451-09-2, .delta.-Aminolevulinic acid hydrochloride 68335-15-9, Photofrin **122341-38-2**, Foscan 129497-78-5, Visudyne **485755-59-7**, Mono-L-aspartyl chlorin e6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(photodynamic therapy pharmacol. aspects, applications and recent advances in drug development)
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L9 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:521933 HCAPLUS
DN 137:108286
TI Antibodies and fragments against epitopes present on cancer, metastatic or leukemia cells and platelets for diagnosis and therapy of tumor, metastasis, leukemia, autoimmune disease, and inflammation
IN Lazarovits, Janette; Hagai, Yocheved; Plaksin, Daniel; Vogel, Tikva; Nimrod, Abraham; Mar-Haim, Hagit; Szanthon, Ester; Richter, Tamar; Amit, Boaz; Kooperman, Lena; Peretz, Tuvia; Levanon, Avigdor
PA Bio-Technology General Corp., USA
SO PCT Int. Appl., 310 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N
CC 15-2 (Immunochemistry)
Section cross-reference(s): 1, 3, 8, 9, 63
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002053700	A2	20020711	WO 2001-US49442	20011231

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-258948P P 20001229
US 2000-751181 A 20001229

AB The present invention provides epitopes present on cancer cells and important in physiol. phenomena such as cell rolling, metastasis, and inflammation. Therapeutic and diagnostic methods and compns. using antibodies capable of binding to the epitopes are provided. The antibodies or fragments are capable of binding to, e.g. PSGL-1, fibrinogen .gamma. prime, GP1b.alpha., heparin, lumican, complement compd. 4 (CC4), interalpha inhibitor and prothrombin. Methods and compns. according to the present invention can be used in diagnosis of and therapy for such diseases as cancer, including tumor growth and metastasis, leukemia, auto-immune disease, and inflammatory disease.
ST antibody fragment epitope cancer metastasis platelet autoimmune disease inflammation
IT Leukemia
(B-cell, acute; antibodies and fragments against epitopes present on cancer, metastatic or leukemia cells and platelets for diagnosis and therapy of tumor, metastasis, leukemia, autoimmune disease, and inflammation)
IT Complement
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CC4; antibodies and fragments against epitopes present on cancer, metastatic or leukemia cells and platelets for diagnosis and therapy of tumor, metastasis, leukemia, autoimmune disease, and inflammation)
IT Antigens
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD162; antibodies and fragments against epitopes present on cancer, metastatic or leukemia cells and platelets for diagnosis and therapy of tumor, metastasis, leukemia, autoimmune disease, and inflammation)
IT Antigens
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)
(CD42; antibodies and fragments against epitopes present on cancer, metastatic or leukemia cells and platelets for diagnosis and therapy of tumor, metastasis, leukemia, autoimmune disease, and inflammation)

IT Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(G; antibodies and fragments against epitopes present on cancer, metastatic or leukemia cells and platelets for diagnosis and therapy of tumor, metastasis, leukemia, autoimmune disease, and inflammation)

IT Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(G; antibodies and fragments against epitopes present on cancer, metastatic or leukemia cells and platelets for diagnosis and therapy of tumor, metastasis, leukemia, autoimmune disease, and inflammation)

IT Glycolipoproteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GPIb.alpha.; antibodies and fragments against epitopes present on cancer, metastatic or leukemia cells and platelets for diagnosis and therapy of tumor, metastasis, leukemia, autoimmune disease, and inflammation)

IT Glycoproteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PSGL-1 (P-selectin glycoprotein ligand-1); antibodies and fragments against epitopes present on cancer, metastatic or leukemia cells and platelets for diagnosis and therapy of tumor, metastasis, leukemia, autoimmune disease, and inflammation)

IT Linking agents
(peptide; antibodies and fragments against epitopes present on cancer, metastatic or leukemia cells and platelets for diagnosis and therapy of tumor, metastasis, leukemia, autoimmune disease, and inflammation)

IT Artery, disease
(**restenosis**; antibodies and fragments against epitopes present on cancer, metastatic or leukemia cells and platelets for diagnosis and therapy of tumor, metastasis, leukemia, autoimmune disease, and inflammation)

IT Eye, disease
(retinopathy; antibodies and fragments against epitopes present on cancer, metastatic or leukemia cells and platelets for diagnosis and therapy of tumor, metastasis, leukemia, autoimmune disease, and inflammation)

IT 442604-60-6 442604-62-8 442604-63-9 442604-64-0 442604-65-1
442604-66-2 442604-67-3 442604-68-4 442604-69-5 442604-70-8
442604-71-9 442604-72-0 442604-73-1 442604-74-2 442604-75-3
442604-76-4 442604-77-5 442604-78-6 442604-79-7 442604-80-0
442604-81-1 442604-82-2 442604-83-3 442604-84-4 442604-85-5
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RL: PRP (Properties)
(unclaimed protein sequence; antibodies and fragments against epitopes present on cancer, metastatic or leukemia cells and platelets for diagnosis and therapy of tumor, metastasis, leukemia, autoimmune disease, and inflammation)

IT 122024-47-9 149298-29-3 245330-86-3 245330-96-5 245331-07-1
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RL: PRP (Properties)
(unclaimed sequence; antibodies and fragments against epitopes present on cancer, metastatic or leukemia cells and platelets for diagnosis and therapy of tumor, metastasis, leukemia, autoimmune disease, and inflammation)

L9 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:449673 HCAPLUS
DN 137:20389
TI Preparation of indenopyrazolone semicarbazides as cyclin dependent kinase inhibitors.
IN Carini, David J.
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D401-12
ICS A61K031-496; A61P035-00; C07D403-12; C07D417-12; C07D407-12; C07D231-54; C07D407-14
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002046182	A1	20020613	WO 2001-US46904	20011207
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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AU 2002028849	A5	20020618	AU 2002-28849	20011207
US 2002091127	A1	20020711	US 2001-10979	20011207
PRAI US 2000-254116P	P	20001208		
WO 2001-US46904	W	20011207		

OS MARPAT 137:20389
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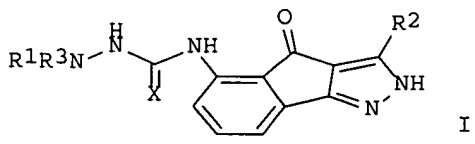

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AB Title compds. [I; X = O, S; R1 = (substituted) carbocyclyl, heterocyclyl; R2 = H, (substituted) alkyl, alkenyl alkynyl, carbocyclyl, heterocyclyl; R3 = H, alkyl, cycloalkyl, cycloalkylalkyl; with provisos], were prepd. as cdk inhibitors (no data). Thus, 3-(4-piperazinophenyl)-5-[[N-methyl-N-(2-pyridinyl)amino]carbamoylamino]indeno[1,2-c]pyrazol-4-1 was prepd. in several steps starting from 4-piperazinoacetophenone.

ST indenopyrazolone semicarbazide prepn cyclin dependent kinase inhibitor; cdk1 inhibitor indenopyrazolone semicarbazide prepn; stenosis treatment indenopyrazolone semicarbazide prepn; anticancer antiviral indenopyrazolone semicarbazide prepn; neurodegeneration treatment indenopyrazolone semicarbazide prepn

IT Artery, disease
(coronary, **restenosis**, treatment; prepn. of indenopyrazolone semicarbazides as cyclin dependent kinase inhibitors)

IT 50-02-2, Dexamethasone 50-07-7, Mitomycin-c 50-18-0, Cyclophosphamide 50-44-2, 6-Mercaptopurine 50-76-0, Dactinomycin 50-91-9, Floxuridine 51-21-8, 5-Fluorouracil 51-75-2, Mechlorethamine 52-24-4, Thiotepa 53-03-2, Prednisone 55-98-1, Busulfan 56-53-1 57-22-7, Vincristine 59-05-2, Methotrexate 125-84-8, Aminoglutethimide 127-07-1, Hydroxyurea 147-94-4, Cytarabine 148-82-3, Melphalan 154-42-7, Thioguanine 154-93-8, Carmustine **305-03-3**, Chlorambucil 427-51-0, Cyproterone acetate 595-33-5, Megestrol acetate 645-05-6, Altretamine 671-16-9, Procarbazine 865-21-4, Vinblastine 2998-57-4, Estramustine 3778-73-2, Ifosfamide 4291-63-8, Cladribine 9015-68-3, Asparaginase 10540-29-1, Tamoxifen 11056-06-7, Bleomycin 13010-47-4, Lomustine 13311-84-7, Flutamide 15663-27-1, Cisplatin 18378-89-7, Plicamycin 18883-66-4, Streptozotocin 20830-81-3, Daunorubicin 21679-14-1, Fludarabine 23214-92-8, Doxorubicin 29767-20-2, Teniposide 33069-62-4, Paclitaxel 33419-42-0, Etoposide 41575-94-4, Carboplatin 53714-56-0, Leuprolide 53910-25-1, Pentostatin 58957-92-9, Idarubicin 61825-94-3, Oxaliplatin 62816-98-2, Tetraplatin 62928-11-4, Iproplatin 65271-80-9, Mitoxantrone 65807-02-5, Goserelin 71486-22-1, Vinorelbine 83150-76-9, Octreotide 88303-60-0, Losoxantrone 90357-06-5, Bicalutamide 91421-42-0, 9-Nitrocamptothecin 91421-43-1, 9-Aminocamptothecin 95058-81-4, Gemcitabine 97682-44-5, Irinotecan 100286-90-6, Cpt-11 114977-28-5, Docetaxel 120511-73-1, Anastrozole 123948-87-8, Topotecan 129580-63-8, JM216 130167-69-0, Pegaspargase 135558-11-1, Lobaplatin 146924-11-0, JM335 264601-43-6, GS-211
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; prepn. of indenopyrazolone semicarbazides as cyclin dependent kinase inhibitors)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Basf Ag; WO 9917769 A 1999 HCAPLUS
(2) Basf Ag; WO 0027822 A 2000 HCAPLUS
(3) Du Pont Pharm Co; WO 9954308 A 1999 HCAPLUS

L9 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:449662 HCAPLUS
DN 137:33310
TI Preparation of anilinopyrimidines as IKK inhibitors
IN Kois, Adam; MacFarlane, Karen J.; Satoh, Yoshitaka; Bhagwat, Shripad S.; Parnes, Jason S.; Palanki, Moorthy S. S.; Erdman, Paul E.
PA Signal Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D239-42
ICS C07D401-12; C07D405-12; C07D413-12; C07D403-12; A61K031-505; A61P029-00
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 10
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002046171	A2	20020613	WO 2001-US46403	20011205
	WO 2002046171	A3	20030123		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
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BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002020195 A5 20020618 AU 2002-20195 20011205

PRAI US 2000-251816P P 20001206

WO 2001-US46403 W 20011205

OS MARPAT 137:33310

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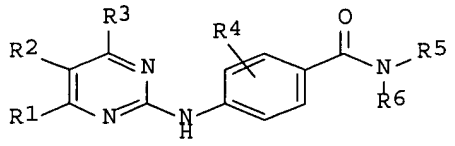


I

AB The title compds. [I; R1 = (un)substituted (hetero)aryl; R2 = H; R3 = H, alkyl; R4 = halo, OH, alkyl, alkoxy; R5, R6 = R8, (CH2)aCOR9, (CH2)aCO2R9, etc.; or NR5R6 = (un)substituted heterocycle; R8, R9 = H, alkyl, aryl, etc.; a = 0-4] having activity as inhibitors of IKK, particularly IKK-2, were prepd. E.g., a multi-step synthesis of I [R1 = 4-ClC6H4; R2-R6 = H] having an IC50 of .ltoreq. 1 .mu.M in the IKK-2 enzyme assay, was given. Such compds. I have utility in the treatment of a wide range of conditions that are responsive to IKK inhibition. Thus, methods of treating such conditions are also disclosed, as are pharmaceutical compns. contg. one or more compds. of the above compds.

ST anilinopyrimidine prepn IKK2 kinase inhibitor; IkappaB protein kinase inhibitor anilino pyrimidine prepn

IT Intestine, disease
(Crohn's; prepn. of anilinopyrimidines as IKK inhibitors)

IT Respiratory distress syndrome
(acute, treatment of; prepn. of anilinopyrimidines as IKK inhibitors)

IT Artery, disease
(coronary, **restenosis**, treatment of **restenosis** following angioplasty; prepn. of anilinopyrimidines as IKK inhibitors)

IT 50-07-7 50-18-0, Cyclophosphamide 50-76-0, Actinomycin D 50-91-9, Floxuridine 51-21-8, 5-Fluorouracil 52-53-9, Verapamil 55-98-1, Busulfan 57-22-7, Vincristine 59-05-2, Methotrexate 70-51-9, Deferoxamine 127-07-1, Hydroxyurea 147-94-4, Cytarabine 154-42-7, Thioguanine 154-93-8, Carmustine 299-75-2, Treosulfan **305-03-3**, Chlorambucil 574-93-6, Phthalocyanine 865-21-4, Vinblastine 3094-09-5, Doxifluridine 3562-63-8, Megestrol 3778-73-2, Ifosfamide 4342-03-4, Dacarbazine 9060-10-0, Bleomycin B2 10540-29-1, Tamoxifen 11116-31-7, Bleomycin A2 13010-47-4, Lomustine 13311-84-7, Flutamide 15663-27-1, Cisplatin 20830-81-3, Daunorubicin 21679-14-1, Fludarabine 22089-22-1, Trofosfamide 23214-92-8, Doxorubicin 24280-93-1, Mycophenolic acid 29767-20-2, Teniposide 31441-78-8, Mercaptopurine 33069-62-4, Paclitaxel 33419-42-0, Etoposide 36791-04-5, Ribavirin 41575-94-4, Carboplatin 48134-75-4, 1-Methyl-4-phenylpyridinium 52128-35-5, Trimetrexate 53643-48-4, Vindesine 54083-22-6, Zorubicin 56420-45-2, Epirubicin 58957-92-9, Idarubicin 60084-10-8, Tiazofurin 62996-74-1, Staurosporine 65271-80-9, Mitoxantrone 67526-95-8, Thapsigargin 68247-85-8, Peplomycin 71486-22-1, Vinorelbine 72496-41-4, Pirarubicin 74381-53-6, Leuprolide acetate 75330-75-5, Lovastatin 84449-90-1, Raloxifene 90357-06-5, Bicalutamide 91421-43-1, 9-Aminocamptothecin 96389-68-3, Crisnatol 118908-07-9, EICAR 123948-87-8, Topotecan 129497-78-5, BPD-MA 131875-08-6, KH 1060 167678-65-1, CB 1093
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticancer agent; prepn. of anilinopyrimidines as IKK inhibitors)

L9 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2003 ACS

AN 2002:449661 HCAPLUS

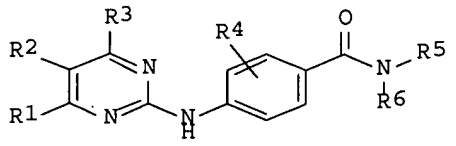
DN 137:33309

TI Preparation of anilinopyrimidines as JNK pathway inhibitors

IN Kois, Adam; MacFarlane, Karen J.; Satoh, Yoshitaka; Bhagwat, Shripad S.; Parnes, Jason S.; Palanki, Moorthy S. S.; Erdman, Paul E.
PA Signal Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D239-00
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 10
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002046170	A2	20020613	WO 2001-US46402	20011205
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002027214	A5	20020618	AU 2002-27214	20011205
PRAI US 2000-251904P	P	20001206		
WO 2001-US46402	W	20011205		

OS MARPAT 137:33309
GI



I

AB The title compds. [I; R1 = (un)substituted (hetero)aryl; R2 = H; R3 = H, alkyl; R4 = halo, OH, alkyl, alkoxy; R5, R6 = R8, (CH2)aCOR9, (CH2)aCO2R9, etc.; or NR5R6 = (un)substituted heterocycle; R8, R9 = H, alkyl, aryl, etc.; a = 0-4] having activity as inhibitors of the JNK pathway, were prepd. E.g., a multi-step synthesis of I [R1 = 4-ClC6H4; R2-R6 = H] having an IC50 of .ltoreq. 10 .mu.M in the JNK2 assay, was given. Such compds. I have utility in the treatment of a wide range of conditions that are responsive to inhibition of the JNK pathway. Thus, methods of treating such conditions are also disclosed, as are pharmaceutical compns. contg. one or more compds. of the above compds.

ST anilinopyrimidine prepn JNK inhibitor

IT Intestine, disease
(Crohn's; prepn. of anilinopyrimidines as JNK pathway inhibitors)

IT Intestine, neoplasm
(colorectal, treatment of; prepn. of anilinopyrimidines as JNK pathway inhibitors)

IT Eye, disease
(conjunctivitis, treatment of; prepn. of anilinopyrimidines as JNK pathway inhibitors)

IT Artery, disease
(coronary, **restenosis**, treatment of **restenosis** following angioplasty; prepn. of anilinopyrimidines as JNK pathway inhibitors)

IT 50-07-7 50-18-0, Cyclophosphamide 50-76-0, Actinomycin D 50-91-9, Floxuridine 51-21-8, 5-Fluorouracil 52-53-9, Verapamil 55-98-1, Busulfan 57-22-7, Vincristine 59-05-2, Methotrexate 70-51-9, Deferoxamine 127-07-1, Hydroxyurea 147-94-4, Cytarabine 154-42-7, Thioguanine 154-93-8, Carmustine 299-75-2, Treosulfan **305-03-3**, Chlorambucil 574-93-6, Phthalocyanine 865-21-4, Vinblastine 3094-09-5, Doxifluridine 3562-63-8, Megestrol 3778-73-2, Ifosfamide 4342-03-4, Dacarbazine 9060-10-0, Bleomycin B2 10540-29-1, Tamoxifen 11116-31-7, Bleomycin A2 13010-47-4, Lomustine 13311-84-7, Flutamide

15663-27-1, Cisplatin 20830-81-3, Daunorubicin 21679-14-1, Fludarabine 22089-22-1, Trofosfamide 23214-92-8, Doxorubicin 24280-93-1, Mycophenolic acid 29767-20-2, Teniposide 31441-78-8, Mercaptopurine 33069-62-4, Paclitaxel 33419-42-0, Etoposide 36791-04-5, Ribavirin 41575-94-4, Carboplatin 48134-75-4, 1-Methyl-4-phenylpyridinium 52128-35-5, Trimetrexate 53643-48-4, Vindesine 54083-22-6, Zorubicin 56420-45-2, Epirubicin 58957-92-9, Idarubicin 60084-10-8, Tiazofurin 62996-74-1, Staurosporine 65271-80-9, Mitoxantrone 67526-95-8, Thapsigargin 68247-85-8, Peplomycin 71486-22-1, Vinorelbine 72496-41-4, Pirarubicin 74381-53-6, Leuprolide acetate 75330-75-5, Lovastatin 84449-90-1, Raloxifene 90357-06-5, Bicalutamide 91421-43-1, 9-Aminocamptothecin 96389-68-3, Crisnatol 118908-07-9, EICAR 123948-87-8, Topotecan 129497-78-5, BPD-MA 131875-08-6, KH 1060 167678-65-1, CB 1093
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticancer agent; prepn. of anilinopyrimidines as JNK pathway inhibitors)

L9 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:636197 HCAPLUS
DN 135:221319
TI Inhibition of integrin by ADAM disintegrin domains and therapeutic uses as angiogenesis inhibitors
IN Fanslow, William C., III; Cerretti, Douglas Pat; Poindexter, Kurt Matthew; Black, Roy A.
PA Immunex Corporation, USA
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N009-64
ICS C12N015-57; A61K038-16; A61P035-00; A61P037-00; A61P027-00; A61P017-02
CC 1-12 (Pharmacology)
Section cross-reference(s): 3, 7, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001062905	A2	20010830	WO 2001-US5701	20010223
WO 2001062905	A3	20020321		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002042368	A1	20020411	US 2001-792200	20010223
EP 1259595	A2	20021127	EP 2001-920133	20010223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI US 2000-184865P	P	20000225		
WO 2001-US5701	W	20010223		

AB The present invention provides methods and compns. for inhibiting the biol. activity of integrins, for inhibiting endothelial cell migration, and for inhibiting angiogenesis. In particular, the invention provides compns. comprising ADAM disintegrin domains and methods for using said compns. as integrin antagonists. DNA and encoded amino acid sequences of fusion proteins contg. ADAM disintegrin domains are provided. In preferred embodiments the methods and compns. of the invention are used to inhibit angiogenesis and to treat diseases or conditions mediated by angiogenesis.
ST integrin antagonist ADAM disintegrin domain angiogenesis inhibitor
IT Artery, disease
(**restenosis**, treatment of; inhibition of integrin by ADAM disintegrin domains and therapeutic uses as angiogenesis inhibitors)
IT 50-07-7 50-18-0, Cyclophosphamide 50-44-2, Mercaptopurine 50-76-0, Dactinomycin 50-91-9, 5-Fluorodeoxyuridine 51-21-8, 5-Fluorouracil 51-75-2, Mechlorethamine 53-19-0, Mitotane 55-98-1, Busulfan 57-22-7, Vincristine 59-05-2, Methotrexate 60-34-4, Methylhydrazine 76-43-7, Fluoxymesterone 127-07-1, Hydroxyurea 147-94-4, Cytarabine

148-82-3, Melphalan 154-42-7, Thioguanine 154-93-8, Carmustine
305-03-3, Chlorambucil 865-21-4, Vinblastine 4342-03-4,
Dacarbazine 7440-06-4D, Platinum, analogs, biological studies
9015-68-3, L-Asparaginase 10540-29-1, Tamoxifen 11056-06-7, Bleomycin
13010-47-4, Lomustine 13909-09-6, Semustine 15663-27-1, Cisplatin
18378-89-7, Plicamycin 18883-66-4, Streptozocin 20830-81-3,
Daunorubicin 23214-92-8, Doxorubicin 29767-20-2, Teniposide
33069-62-4, Taxol 33419-42-0, Etoposide 41575-94-4, Carboplatin
53643-48-4, Vindesine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment by ADAM disintegrin domains and; inhibition of integrin by
ADAM disintegrin domains and therapeutic uses as angiogenesis
inhibitors)

L9 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:63858 HCAPLUS
DN 134:125935
TI Methods for treatment of hyperproliferative diseases using human MDA-7
IN Mhashilkar, Abner; Schrock, Bob; Chada, Sunil
PA Introgen Therapeutics, Inc., USA
SO PCT Int. Appl., 161 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K048-00
CC 1-6 (Pharmacology)
Section cross-reference(s): 3, 14, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001005437	A2	20010125	WO 2000-US19392	20000713
WO 2001005437	A3	20030206		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-144354P P 19990715
US 2000-200768P P 20000428

AB The present invention relates to gene therapy methods for the treatment of human disease. More specifically, the invention is directed, in one embodiment, to methods for treating a subject with a hyperproliferative disease. In another embodiment, an adenoviral expression construct comprising a nucleic acid encoding a human MDA-7 protein under the control of a promoter operable in eukaryotic cells is administered to the patient with a hyperproliferative disease. The present invention thus provides a gene therapy for treating hyperproliferative disease by elevating the expression of MDA-7 resulting in inhibition of cell growth and induction of apoptosis in hyperproliferative cells.
ST human protein MDA7 sequence hyperproliferative disease gene therapy
IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MDA-7; methods for treatment of hyperproliferative diseases using human MDA-7)
IT Artery, disease
(**restenosis**, inhibitors; methods for treatment of hyperproliferative diseases using human MDA-7)
IT 50-18-0, Cyclophosphamide 51-75-2, Mechlorethamine 55-98-1, Busulfan
57-22-7, Vincristin 59-05-2, Methotrexate 148-82-3, Melphalan
305-03-3, Chlorambucil 671-16-9, Procarbazine 865-21-4,
Vinblastin 3778-73-2, Ifosfamide 10540-29-1, Tamoxifen 11056-06-7,
Bleomycin 13010-20-3, Nitrosurea 14913-33-8, Transplatin 18378-89-7,
Plicamycin 20830-81-3, Daunorubicin 23214-92-8, Doxorubicin
33069-62-4, Taxol 41575-94-4, Carboplatin 114977-28-5, Taxotere
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(for chemotherapy; methods for treatment of hyperproliferative diseases

using human MDA-7)

IT 57-88-5, Cholesterol, biological studies 144189-73-1, DOTAP
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lipoplex comprising; methods for treatment of hyperproliferative diseases using human MDA-7)

IT 167679-53-0P, Protein (human gene mda-7)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; methods for treatment of hyperproliferative diseases using human MDA-7)

IT 321890-89-5
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; methods for treatment of hyperproliferative diseases using human MDA-7)

L9 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:573656 HCAPLUS
DN 133:182982
TI Alkylating agents for treatment of cellular proliferation
IN Alvarado, Angelica; Eury, Robert; Pomerantseva, Irina D.; Froix, Michael
PA Quanam Medical Corporation, USA
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000047197	A2	20000817	WO 2000-US3667	20000210
	WO 2000047197	A3	20010405		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1150670	A2	20011107	EP 2000-914574	20000210
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002536406	T2	20021029	JP 2000-598150	20000210
PRAI	US 1999-119951P	P	19990212		
	WO 2000-US3667	W	20000210		

AB A method of inhibiting cell proliferation assocd. with a hyperproliferative condition, such as **restenosis**, is described. The method includes administering an alkylating agent. A stent for local administration of the alkylating agent is also described. A polymer stent was prepd. according to the following procedure. Bu methacrylate, hexanediol dimethacrylate, Me methacrylate, and PEG methacrylate were mixed and polymd. between glass plates to form thin films. Prior to polymn., gold strips were placed at intervals to provide for radio-opacity of the stents. After polymn., the film was cut into V-shaped strips by using a punch and any unpolymd. monomer was removed by solvent extn. The selected drug was loaded into the polymer stent by prepg. a soln. of the drug in a suitable solvent, (isopropanol or methanol), N-methylpyrrolidone or DMF. The stent was weighed and placed in a clean container. A known vol. of the drug soln. was pipetted over the surface of the stent. The stent was then placed in a vacuum oven at about 40.degree. for 1-3 days to dry.

ST alkylating agent cell proliferation polymer stent

IT Alkylating agents, biological
Cell proliferation
Microtubule
(alkylating agents for treatment of cellular proliferation)

IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(alkylating agents for treatment of cellular proliferation)
IT Medical goods
(catheters; alkylating agents for treatment of cellular proliferation)
IT Artery, disease
(coronary, **restenosis**; alkylating agents for treatment of cellular proliferation)
IT Chloramines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitrogen mustards; alkylating agents for treatment of cellular proliferation)
IT Medical goods
(stents; alkylating agents for treatment of cellular proliferation)
IT 253325-95-0P 284665-59-4P
RL: DEV (Device component use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(alkylating agents for treatment of cellular proliferation)
IT 50-02-2, Dexamethasone 52-53-9, Verapamil 55-98-1, Busulfan 64-86-8, Colchicine 148-82-3, Melphalan 154-93-8, Carmustine **305-03-3**, Chlorambucil 13010-20-3D, Nitrosourea, derivs. 33069-62-4, Paclitaxel
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkylating agents for treatment of cellular proliferation)

L9 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 1999:48609 HCAPLUS
DN 130:119591
TI Antioxidant enhancement of therapy for hyperproliferative conditions
IN Chinery, Rebecca; Beauchamp, R. Daniel; Coffey, Robert J.; Medford, Russell M.; Wadsinski, Brian
PA Atherogenics, Inc., USA
SO PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
CC 1-6 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9901118	A2	19990114	WO 1998-US13750	19980701
	WO 9901118	A3	19990422		
	W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9882827	A1	19990125	AU 1998-82827	19980701
	EP 1019034	A2	20000719	EP 1998-933078	19980701
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002511878	T2	20020416	JP 1999-507360	19980701
	US 2001049349	A1	20011206	US 2001-779086	20010207
PRAI	US 1997-886653	A	19970701		
	US 1997-967492	A	19971111		
	US 1998-108609	B1	19980701		
	WO 1998-US13750	W	19980701		

OS MARPAT 130:119591
AB A method to enhance the cytotoxic activity of an antineoplastic drug comprises administering an effective amt. of the antineoplastic drug to a host exhibiting abnormal cell proliferation in combination with an effective cytotoxicity-increasing amt. of an antioxidant. The invention also includes a method to decrease the toxicity to an antineoplastic agent or increase the therapeutic index of an antineoplastic agent administered for the treatment of a solid growth of abnormally proliferating cells, comprising administering an antioxidant prior to, with, or following the antineoplastic treatment.
ST hyperproliferation disorder drug enhancement antioxidant; antineoplastic drug enhancement antioxidant
IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(17-1A; antioxidant enhancement of therapy for hyperproliferative conditions)

IT Artery
(angioplasty, **restenosis** after; antioxidant enhancement of therapy for hyperproliferative conditions)

IT Lymphocyte
(antilymphocyte Igs; antioxidant enhancement of therapy for hyperproliferative conditions)

IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antilymphocyte; antioxidant enhancement of therapy for hyperproliferative conditions)

IT Artery, disease
(**restenosis**, post-angioplasty; antioxidant enhancement of therapy for hyperproliferative conditions)

IT 50-18-0, Cyclophosphamide 50-44-2, Mercaptopurine 50-76-0, Dactinomycin 50-81-7, Vitamin C, biological studies 50-91-9, Floxuridine 51-21-8, 5-Fluorouracil 52-24-4, Thiotepa 53-19-0, Mitotane 54-91-1, Pipobroman 55-86-7, Mustine hydrochloride 55-98-1, Busulphan 59-05-2, Methotrexate 59-14-3, Broxuridine 66-75-1, Uramustine 125-84-8, Aminoglutethimide 127-07-1, Hydroxyurea 143-67-9, Vinblastine sulfate 147-94-4, Cytarabine 148-82-3, Melphalan 154-42-7, Thioguanine 154-93-8, Carmustine 299-75-2, Treosulfan **305-03-3**, Chlorambucil 320-67-2, Azacitidine 366-70-1, Procarbazine hydrochloride 446-86-6, Azathioprine 488-41-5, Mitobronitol 512-64-1, Echinomycin 566-48-3, Formestane 574-25-4, Thioinosine 594-07-0D, Carbamodithioic acid, derivs. 616-91-1, N-Acetylcysteine 642-83-1, Aceglatone 645-05-6, Altretamine 968-93-4, Testolactone 1404-00-8, Mitomycin 1406-18-4, Vitamin E 1954-28-5, Ethoglucid 2068-78-2, Vincristine sulfate 2353-33-5,

L9 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:527193 HCAPLUS
DN 129:166193
TI Therapeutic treatment and prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix
IN Setterstrom, Jean A.; Van Hamont, John E.; Reid, Robert H.; Jacob, Elliot; Jeyanthi, Ramasubbu; Boedeker, Edgar C.; McQueen, Charles E.; Tice, Thomas R.; Roberts, F. Donald; Friden, Phil
PA United States Dept. of the Army, USA; Van Hamont, John E.; et al.
SO PCT Int. Appl., 363 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-52
ICS A61K047-30
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 2, 15
FAN.CNT 12

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9832427	A1	19980730	WO 1998-US1556	19980127
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6309669	B1	20011030	US 1997-789734	19970127
AU 9863175	A1	19980818	AU 1998-63175	19980127
PRAI US 1997-789734	A	19970127		
US 1984-590308	B1	19840316		
US 1992-867301	A2	19920410		
US 1995-446148	A2	19950522		

US 1995-446149 B2 19950522
US 1996-590973 B2 19960124
WO 1998-US1556 W 19980127

AB Novel burst-free, sustained release biocompatible and biodegradable microcapsules are disclosed which can be programmed to release their active core for variable durations ranging from 1-100 days in an aq. physiol. environment. The microcapsules are comprised of a core of polypeptide or other biol. active agent encapsulated in a matrix of poly(lactide/glycolide) copolymer, which may contain a pharmaceutically acceptable adjuvant, as a blend of upcapped free carboxyl end group and end-capped forms ranging in ratios from 100/0 to 1/99.

ST infection microcapsule sustained release peptide copolymer

IT Artery, disease
(**restenosis**; prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT 50-06-6, Phenobarbital, biological studies 50-12-4, Mephenytoin 50-18-0, Cyclophosphamide 50-23-7, Hydrocortisone 50-24-8, Prednisolone 50-28-2, 17.beta.-Estradiol, biological studies 50-33-9, Phenylbutazone, biological studies 50-52-2, Thioridazine 50-55-5, Reserpine 50-78-2, Aspirin 51-55-8, Atropine, biological studies 52-24-4, Thiotepa 52-76-6, Lynestrenol 53-03-2, Prednisone 53-16-7, Estrone, biological studies 53-86-1, Indomethacin 54-11-5, Nicotine 55-48-1, Atropine sulfate 55-63-0, Nitroglycerin 55-86-7, Nitrogen mustard 56-53-1, Diethyl stilbestrol **56-75-7**, Chloramphenicol 57-27-2, Morphine, biological studies 57-33-0, Sodium pentobarbital 57-42-1, Meperidine 57-53-4, Meprobamate 57-63-6, Ethinyl estradiol 57-85-2, Testosterone propionate 57-92-1, Streptomycin a, biological studies 58-08-2, Caffeine, biological studies 58-14-0, Pyrimethamine 58-22-0 58-25-3, Chlordiazepoxide 58-39-9, Perphenazine 58-73-1, Diphenhydramine 59-01-8, Kanamycin a 59-05-2, Methotrexate 59-92-7, L-Dopa, biological studies 61-33-6, Penicillin g, biological studies 67-20-9, Nitrofurantoin 68-22-4, Norethisterone 68-23-5, Norethynodrel 69-09-0, Chlorpromazine hydrochloride 69-53-4, Ampicillin 69-72-7D, Salicylic acid, derivs. 71-58-9, Medroxyprogesterone acetate 72-33-3, Mestranol 76-57-3, Codeine 79-57-2, Oxytetracycline 79-64-1, Dimethisterone 91-81-6, Tripelennamine 103-90-2, Acetaminophen 113-15-5, Ergotamine 114-07-8, Erythromycin 114-49-8, Hyoscine hydrobromide 121-54-0 122-09-8, Phentermine 125-29-1, Dihydrocodeinone 125-71-3, Dextromethorphan 127-48-0, Trimethadione 128-62-1, Noscapine **145-94-8**, Chlorindanol 148-82-3, Melphalan 155-41-9, Methscopolamine bromide 288-32-4D, Imidazole, derivs. 297-76-7, Ethynodiol diacetate 302-22-7, Chlormadinone acetate **305-03-3**, Chlorambucil 309-43-3, Sodium secobarbital

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Jeyanthi; Proceedings International Symposium on Controlled Release of Bioactive Materials 1996, P351 HCAPLUS
(2) Oppenheim; US 5486503 A 1996 HCAPLUS
(3) Syntex U S AInc; EP 0052510 B2 1994 HCAPLUS
(4) Wang; J of Controlled Release 1991, V17, P23 HCAPLUS
(5) Yan; J of Controlled Release 1994, V32(3), P231 HCAPLUS
(6) Yeh; A Novel Emulsification-Solvent Extraction Technique for Production of Protein Loaded Biodegradable Microparticles for Vaccine and Drug Delivery 1995, V33(3), P437 HCAPLUS

L9 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2003 ACS
AN 1996:754393 HCAPLUS
DN 126:102570
TI Reporter gene methods for identification of compounds that modulate transcription of genes associated with cardiovascular disease
IN Foulkes, J. Gordon; Liechtfried, Franz E.; Pieler, Christian; Stephenson, John R.; Case, Casey C.
PA Oncogene Science, Inc., USA
SO U.S., 93 pp., Cont.-in-part of U.S. Ser. No. 555,196, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM C12P019-34
ICS C12Q001-68
NCL 435006000
CC 14-5 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 1, 3

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5580722	A	19961203	US 1992-832905	19920207
	US 6203976	B1	20010320	US 1994-255236	19940607
	US 5665543	A	19970909	US 1994-267834	19940628
	US 6165712	A	20001226	US 1995-463691	19950605
	US 5976793	A	19991102	US 1996-683455	19960718
	US 5846720	A	19981208	US 1996-700757	19960815
	US 5863733	A	19990126	US 1997-779230	19970106
	US 6136779	A	20001024	US 1997-778754	19970106
	US 6376175	B1	20020423	US 1998-123728	19980728
PRAI	US 1989-382712	B2	19890718		
	US 1990-555196	B2	19900718		
	US 1991-644233	B1	19910118		
	US 1992-832905	A1	19920207		
	US 1993-13343	B1	19930204		
	US 1993-134215	B1	19931008		
	US 1994-255236	A3	19940607		
	US 1994-267834	A1	19940628		
	US 1996-683455	A1	19960718		

AB Reporter genes and hybridization assays are used to screen and identify compds. that modulate the transcription of a gene encoding a protein of interest assocd. with treatment of one or more symptoms of a cardiovascular disease such as atherosclerosis, **restenosis** or hypertension. The compds. identified can be used therapeutically in the modulation of transcription of human genes encoding a proteins of interest assocd. with treatment of one or more symptoms of a cardiovascular disease, thus ameliorating the disease. Construction of reporter gene constructs using promoters from a no. of genes assocd. with cardiovascular disease to drive a luciferase gene using animal cell hosts is described. Results from a preliminary high throughput screen identified a no. of chems. inducing the granulocyte colony-stimulating factor gene.

ST cardiovascular disease gene expression regulation; effector cardiovascular disease gene expression regulation

IT Artery, disease
(coronary, **restenosis**; reporter gene methods for identification of compds. that modulate transcription of genes assocd. with cardiovascular disease)

IT 52-21-1, Prednisolone 21-acetate **56-75-7**, Chloramphenicol 76-25-5, Triamcinolone acetonide 93-40-3, Homoveratric acid 153-78-6, 2-Aminofluorene 822-87-7, 2-Chlorocyclohexanone 1107-26-2, .beta.-Apo-8'-carotenal 1148-79-4, 2,2':6',2''-Terpyridine 2051-98-1, 5-Bromoacenaphthene 2227-13-6 3096-57-9, 2-Amino-9-fluorenone 5413-85-4, 5-Amino-4,6-dichloropyrimidine 17687-22-8, 5-Iodoorotic acid 36192-63-9, 2-Amino-4'-methylbenzophenone 52698-84-7, Bathocuproinedisulfonic acid disodium salt 88404-25-5, 4-(Bromomethyl)-6,7-dimethoxy coumarin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(induction of mouse mammary tumor virus gene expression by; reporter gene methods for identification of compds. that modulate transcription of genes assocd. with cardiovascular disease)

=> s l4 and l6
L10 58 L4 AND L6

=> d ibib abs 55-58

L10 ANSWER 55 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:490263 HCAPLUS
DOCUMENT NUMBER: 119:90263
TITLE: Chloroaluminum sulfonated phthalocyanine partitioning in normal and intimal hyperplastic artery in the rat: implications for **photodynamic therapy**
AUTHOR(S): LaMuraglia, Glenn M.; Ortu, Paolo; Flotte, Thomas J.; Roberts, W. Gregory; Schomacker, Kevin T.; ChandraSekar, N. R.; Hasan, Tayyaba
CORPORATE SOURCE: Vasc. Surg. Div., Massachusetts Gen. Hosp., Boston, MA, 02114, USA

SOURCE: American Journal of Pathology (1993), 142(6), 1898-905
CODEN: AJPAA4; ISSN: 0002-9440
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Photodynamic therapy**, the light activation of photosensitizers into cytotoxic mediators, has been a successful treatment for exptl. **intimal hyperplasia** (IH). To understand the basis of the photosensitizer chloroaluminum sulfonated phthalocyanine (CASPc)-mediated photoinhibition of **intimal hyperplasia** in the rat common carotid artery model, photosensitizer partitioning was studied in hyperplastic as compared to normal arterial tissue. Serum clearance of CASPc is exponential with, a half-life of 300 min. Laser-induced fluorescence and spectrofluorometric analyses of artery tissue demonstrated an .apprx.60% lower uptake and retention of CASPc by normal arterial tissue as compared to arteries with IH; the differences become more pronounced at 24 h. Fluorescent microscopy of arterial tissue demonstrated increased uptake of the CAPSc by the artery with IH. However, by 24 h it was primarily the IH tissue that had retained the CASPc, with clearance of the dye from the media of normal or hyperplastic arteries. These data demonstrate that IH, like neoplastic tissue, has an increased accumulation of CASPc compared to normal artery. The preferential partitioning into hyperplastic tissue has implications for therapeutic targeting of this cellular population with **photodynamic therapy**.

L10 ANSWER 56 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:119969 HCAPLUS
DOCUMENT NUMBER: 118:119969
TITLE: Inhibition of **intimal hyperplasia** by **photodynamic therapy** using Photofrin
AUTHOR(S): Eton, Darwin; Colburn, Michael D.; Shim, Veronica; Panel, William; Lee, David; Moore, Wesley S.; Ahn, Samuel
CORPORATE SOURCE: Cent. Health Sci., UCLA, Los Angeles, CA, 90024-6904, USA
SOURCE: Journal of Surgical Research (1992), 53(6), 558-62
CODEN: JSGRA2; ISSN: 0022-4804
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Photodynamic therapy** using Photofrin and light energy inhibits human myofibroblast proliferation in cell culture. The purpose of this study is to evaluate its influence on **intimal hyperplasia** in vivo. Twenty New Zealand white rabbits underwent a standardized intimal injury to both common carotid arteries with a 2 Fr balloon catheter. One week later, half of the animals received Photofrin (5 mg/kg) i.v. The remaining 10 rabbits received no Photofrin. Two days later, all neck incisions were reopened and a 1-cm segment of each of the 40 carotid arteries was exposed for 5 min to 80 mW of 630 nm light energy from a continuous wave tunable dye laser (fluence = 7.6 J/cm2). All vessels were harvested 5 wk post-laser treatment following in vivo fixation with formalin. From each artery, sep. cross-sections taken from both the lasered and nonlasered regions of each vessel were mounted and stained for histol. evaluation. Analyzed segments were then divided into 4 different treatment groups: group I segments consisted of arterial cross-sections which were taken from vessel regions that were injured but received neither Photofrin nor laser treatment (group I, n = 20); group II segments also did not receive Photofrin but were exposed to light energy (group II, n = 20); group III segments received Photofrin but no light energy (group III, n = 20); and cross-sections in group IV were taken from those segments which received both Photofrin and laser treatment. Using planimetry, the ratio of the area of **intimal hyperplasia** (IH) to the area enclosed by the internal elastic lamina (IEL) was measured for each specimen (IH/IEL). The mean IH/IEL ratio, expressed as a percent, for control group I segments was 28.1. Regions exposed to light energy or Photofrin alone had a mean value of 22.2 and 22.3, resp. Finally, those segments which received both Photofrin and laser treatment had a IH/IEL ratio of 15.9. The difference between the arterial segments which were exposed to both Photofrin and laser treatment, and those which received neither, is statistically significant ($P < 0.01$). It is concluded that **photodynamic therapy** using Photofrin and 630 nm light, administered 1 wk following a carotid endothelial injury, inhibits **intimal hyperplasia** in rabbits.

L10 ANSWER 57 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:18587 HCAPLUS
DOCUMENT NUMBER: 118:18587
TITLE: Photochemical effects of chloroaluminumsulfonated phthalocyanine in arteries with **intimal hyperplasia**
AUTHOR(S): Ortu, Paolo; LaMuraglia, Glenn M.; Roberts, W. Gregory; Schomacker, Kevin T.; Deutsch, Thomas F.; Flotte, Thomas J.; Hasan, Tayyaba
CORPORATE SOURCE: Wellman Lab. Photomed., Massachusetts Gen. Hosp., Boston, MA, USA
SOURCE: Proceedings of SPIE-The International Society for Optical Engineering (1992), 1646(Proc. Laser-Tissue Interact. III, 1992), 188-94
CODEN: PSISDG; ISSN: 0277-786X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study uses **photodynamic therapy** (**PDT**) for the treatment of **intimal hyperplasia** (IH) in the rat carotid artery model, using chloroaluminumsulfonated phthalocyanine.

L10 ANSWER 58 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:467617 HCAPLUS
DOCUMENT NUMBER: 115:67617
TITLE: **Photodynamic therapy** of vascular stenoses? Response of cultured human smooth muscle cells from non-atherosclerotic arteries and atheromatous plaques following treatment with photosensitizing porphyrins
AUTHOR(S): Dartsch, P. C.; Voisard, R.; Ischinger, T..; Coppenrath, K.; Unger, F.; Hutter, J.; Gottschalk, W.; Unsoeld, E.
CORPORATE SOURCE: Tuebingen, Germany
SOURCE: Proceedings of SPIE-The International Society for Optical Engineering (1990), 1462(Ger. Symp. Laser Angioplasty, 2nd, 1989), 77-80
CODEN: PSISDG; ISSN: 0277-786X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of dihematoporphyrin ester/ether (DHE), a photosensitizing porphyrin with different amts. of aggregates, on the growth and viability of cultured smooth muscle cells obtained from nonatherosclerotic arteries (nor-SMC) and from atheromatous plaques (pla-SMC) was examd. without and with photoactivation of the drug. The results demonstrate that DHE accumulated to a greater extent in plaque-derived cells than in nor-SMC. Even without photoactivation, DHE decreased the proliferative activity of pla-SMC. Photoradiation of porphyrin-labeled cells resulted in a more pronounced sensitivity of pla-SMC when compared with nor-SMC. Morphol. alterations caused by photodynamic reaction finally resulted in a lysis of the cells. In addn., by use of immunofluorescence microscopy, a no. of cytoskeletal alterations such as a depolymn. of stress fibers and microtubules following DHE-labeling and photoradiation were obsd. Since pla-SMC were considerably more sensitive against DHE treatment than nor-SMC in all expts., this drug seems to be potentially valuable as a therapeutic approach to vascular stenoses to reduce **restenosis** rates after angioplasty.

=> d ibib abs 45-48

L10 ANSWER 45 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:584902 HCAPLUS
DOCUMENT NUMBER: 125:241929
TITLE: Tin ethyl etiopurpurin significantly inhibits vascular smooth muscle cell proliferation in vivo
AUTHOR(S): Coats, William D., Jr.; Currier, Jesse W.; Mejias, Yvonne; Narciso, Hugh L.; Faxon, David P.
CORPORATE SOURCE: Department Medicine, Division Cardiology, University Southern California School Medicine, Los Angeles, CA, 90033, USA
SOURCE: Biochemistry and Cell Biology (1996), 74(3), 325-331

CODEN: BCBIEQ; ISSN: 0829-8211
PUBLISHER: National Research Council of Canada
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Smooth muscle cell proliferation is a major component of **restenosis** following angioplasty. Hematoporphyrin deriv. and other photosensitive compds. inhibit proliferation by causing cellular necrosis upon light activation (**photodynamic therapy**). Other photosensitive compds., such as benzoporphyrin deriv., have been suggested as having non-cytotoxic antiproliferative effects without **photodynamic therapy**, although other studies using benzoporphyrin deriv. were neg. Inhibition of smooth muscle cell proliferation was examd. in an in vivo rabbit model of vascular injury using a novel synthetic chlorin deriv., tin Et etiopurpurin, and benzoporphyrin deriv. without **photodynamic therapy**. Tin Et etiopurpurin and benzoporphyrin deriv. inhibited smooth muscle cell proliferation by 50-90% of control (p .ltoreq. 0.05) without toxic side effects. These results suggest that tin Et etiopurpurin and benzoporphyrin deriv. without **photodynamic therapy** may provide a novel and potent antiproliferative therapy that might be useful in the treatment of **restenosis**.

L10 ANSWER 46 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:434564 HCAPLUS
DOCUMENT NUMBER: 125:136570
TITLE: Effects of benzoporphyrin derivative monoacid on balloon injured arteries in a swine model of **restenosis**
AUTHOR(S): Vincent, G. Michael; Fox, Jolene; Johnson, Suzanne; Maragon, Phillipe
CORPORATE SOURCE: LDS Hospital, Salt Lake City, UT, USA
SOURCE: Proceedings of SPIE-The International Society for Optical Engineering (1996), 2671(Lasers in Surgery: Advanced Characterization, Therapeutics, and Systems VI), 72-77
CODEN: PSISDG; ISSN: 0277-786X
PUBLISHER: SPIE-The International Society for Optical Engineering
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We evaluated Benzoporphyrin Deriv. Verteporfin (BPD) **Photodynamic Therapy** (**PDT**) and dark effect on the intima (I) and media (M) hyperplasia (H) response of swine iliac arteries to balloon dilatation (Bdil) injury. Four month old Yucatan swine received bdil at 8 ATM pressure to all four iliac arteries. Pigs were randomly assigned to groups as shown below. **PDT** was performed with intraluminal 690 nm, CW laser (200 mW and 30 J per cm2 tissue). Six weeks later, sites were pressure fixed, and excised at autopsy. Sections from each site were evaluated for I and M thickness, injury score (1 = normal, 4 = worst), and smooth muscle cell (SMC) intensity and distribution. Groups were compared using the Mann-Whitney U test. Means for each parameter were detd., and group means used for statistical anal. Bdil produced IH and MH. **PDT** enhanced IH. BPF at 2 mg/kg reduced MH and produced a favorable trend in IH and Injury. No differences in SMC intensity and distribution were present.

L10 ANSWER 47 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:322855 HCAPLUS
DOCUMENT NUMBER: 125:4594
TITLE: Prevention of late lumen loss after coronary angioplasty by **photodynamic therapy** : role of activated neutrophils
AUTHOR(S): Sluiter, Wim; de Vree, Wil J. A.; Pietersma, Anneke; Koster, Johan F.
CORPORATE SOURCE: Faculty of Medicine and Health Sciences, Erasmus University, Rotterdam, 3000 DR, Neth.
SOURCE: Molecular and Cellular Biochemistry (1996), 157(1&2), 233-238
CODEN: MCBIB8; ISSN: 0300-8177
PUBLISHER: Kluwer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Restenosis** after coronary angioplasty arises from fibrocellular **intimal hyperplasia** and possibly failure of the artery

to enlarge adequately. Which mechanisms underlie this process is only partly understood. No drugs have been clin. effective in reducing the incidence of **restenosis**. Since recently, **photodynamic therapy** (**PDT**) is being investigated as a possible treatment for **intimal hyperplasia**. **PDT** involves the systemic administration of a light-excitable photosensitizer that is taken up rather preferentially by rapidly proliferating cells. During laser irradn. light energy is transferred from the photosensitizer to oxygen generating the highly reactive singlet oxygen. This potent oxidizer can cause severe cellular damage. After **PDT** of a balloon-injected artery from the rat and rabbit the media remained acellular for several weeks to months, and **intimal hyperplasia** did not occur. The endothelial lining regenerated by two weeks, but why smooth muscle cells did not repopulate the media is not known. Neutrophils seem to play an important role in the prevention of **restenosis** after coronary angioplasty, since the activation status of this type of phagocyte is directly related to vessel diam. at late follow-up. Furthermore, it has been obsd. that neutrophils adhere to the microvascular wall upon **PDT** in vivo. In vitro findings suggest that the increased neutrophil adherence was not dependent on a decreased release of the anti-adhesive factors NO and prostacyclin by the **PDT**-treated endothelial cells. Furthermore, **PDT** did not stimulate the expression of P-selectin by the endothelial cells, one of the adhesion receptors for neutrophils. The endothelial cells only retract upon **PDT** allowing the adherence of neutrophils by their .beta.2-integrin adhesion receptors to the subendothelial matrix. On the basis of these findings, we presume that the successful prevention of **intimal hyperplasia** by **PDT** partly depends on the presence of the neutrophil at the site of the lesion.

L10 ANSWER 48 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:955385 HCAPLUS
DOCUMENT NUMBER: 124:49674
TITLE: **Photodynamic therapy**: Cytotoxicity of aluminum phthalocyanine on **intimal hyperplasia**
AUTHOR(S): Eton, Darwin; Borhani, Martin; Spero, Kenneth; Cava, Raymond A.; Grossweiner, Leonard; Ahn, Samuel S.
CORPORATE SOURCE: Departments Surgery, University Illinois, Chicago, IL, USA
SOURCE: Archives of Surgery (Chicago) (1995), 130(10), 1098-103
CODEN: ARSUAX; ISSN: 0004-0010
PUBLISHER: American Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The objective was to study the cytotoxic effect of **photodynamic therapy** (**PDT**) on myointimal hyperplasia (MIH) in 120 New Zealand white rabbits using the chromophore chloroaluminum phthalocyanine tetrasulfonate (APtS). A common carotid artery (CCA) injury model was used to initiate MIH. **Photodynamic therapy** was administered 1 wk after injury (inhibition arm) or 6 wk after injury (treatment arm). The inhibition arm CCAs were harvested 6 wk after therapy. The treatment arm CCAs were harvested 1 wk or 6 wk after therapy. Each evaluation included four subgroups (n=10 each): control, drug only, laser only, and drug plus laser. An established CCA balloon injury model was used. **Photodynamic therapy** was administered by exposing CCAs to continuous external laser irradn. 30 min after treatment with a 2.5-mg/kg i.v. dose of APtS (fluence=25 J/cm2, .lambda.=672 nm). The control and drug-only subgroups received sham reoperations without laser exposure. Following harvest, the CCAs were evaluated for area of stenosis and cell d. In the inhibition arm, no **PDT** effect was seen on intimal cell d. or area stenosis. In the treatment arm, intimal cell d. was markedly diminished (P<.05) in the rabbits in the drug-laser group that were killed 1 wk but not 6 wk after **PDT** compared with rabbits in the control, drug-only, and laser-only groups. Area stenosis was not significantly affected by **PDT**. Marked acute cytotoxicity of **PDT** on MIH was verified in vivo in the treatment arm. No sustained benefit of **PDT** was seen in the inhibition or the treatment arms. Refinements in dosimetry will be necessary to achieve long-term benefit of **PDT** for MIH.

=> d ibib abs 40-43

L10 ANSWER 40 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:605535 HCAPLUS
DOCUMENT NUMBER: 127:231333
TITLE: **Photodynamic therapy** inactivates cell-associated basic fibroblast growth factor: a silent way of vascular smooth muscle cell eradication
AUTHOR(S): Van Eps, Randolph G. Statius; Adili, Farzin; Lamuraglia, Glenn M.
CORPORATE SOURCE: Division of Vascular Surgery and Wellman Laboratories of Photomedicine, Harvard Medical School, Massachusetts General Hospital, Boston, MA, 02114, USA
SOURCE: Cardiovascular Research (1997), 35(2), 334-340
CODEN: CVREAU; ISSN: 0008-6363
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Procedurally related vascular injury results in a smooth muscle cell (SMC) proliferative response which is in part initiated by SMC release of mitogens, including basic fibroblast growth factor (bFGF). This injury-induced proliferative response is believed to be a key event in **intimal hyperplasia** development. **Photodynamic therapy** (**PDT**), a novel approach found to be effective in inhibiting exptl. **intimal hyperplasia**, produces cytotoxic free radicals resulting in localized SMC eradication. However, this form of SMC injury does not induce an inflammatory or proliferative response in the vessel wall. This study investigated whether **PDT** -generated free radicals could inactivate cell-assocd. bFGF normally released with cell injury. **PDT** of bovine SMC was performed in vitro with the photosensitizer CASPc (5 .mu.g/mL) and 675 nm laser light using three different fluences: 10, 50, and 100 J/cm2. After **PDT** , SMC viability was detd. with the tetrazolium salt (MTT) assay and cell-assocd. bFGF was quantitated by ELISA. A SMC mitogenesis assay was utilized to detect cell-assocd. bFGF activity released with SMC injury. In a dose-dependent manner, **PDT**-generated free radicals reduced cell-assocd. bFGF levels. After **PDT** with 100 J/cm2, cell-assocd. bFGF content was reduced by 88% ($P < 0.0002$). Of special interest was the finding that **PDT** with 10 J/cm2 significantly ($P < 0.0002$) reduced cell viability to around 50%, without affecting cellular bFGF levels. Consequently, a higher **PDT** dose (100 J/cm2) was needed to significantly ($P < 0.001$) inhibit the SMC mitogenic response assocd. with SMC injury. These results provide a mechanism to explain how, unlike mech. or other forms of SMC injury, optimal doses of **PDT** can locally eradicate medial vascular SMC without resulting in a bFGF-induced initiation of cell proliferation.

L10 ANSWER 41 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:387064 HCAPLUS
DOCUMENT NUMBER: 127:77968
TITLE: Effect of **photodynamic therapy** in **intimal hyperplasia** by phthalocyanine conjugated to the scavenger-receptor ligand, maleylated bovine serum albumin
AUTHOR(S): Ito, Shigeki; Nagae, Tsuneyuki; Ishimaru, Shin; Chau, Sara; Dang, Triet; Sabiniano, Leslie Anne.; Zempo, Mizuho; Booth, Mark C.; Liaw, Lih-Huei L.; et al.
CORPORATE SOURCE: Department of Surgery, Tokyo Medical College, Tokyo, Japan
SOURCE: Proceedings of SPIE-The International Society for Optical Engineering (1997), 3033(Physiology and Function from Multidimensional Images), 280-296
CODEN: PSISDG; ISSN: 0277-786X
PUBLISHER: SPIE-The International Society for Optical Engineering
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Intimal hyperplasia** (IH) is major cause of **restenosis** after vascular interventions for arterial occlusive disease. We reported that a fluorescenct probe, Texas Red, conjugated to the scavenger-receptor ligand, maleylated bovine serum albumin (mal-BSA), accumulated almost exclusively in the injured, hyperplastic sites. The purpose of this study is to test the feasibility of enhanced drug delivery

to the hyperplastic lesion by targeting the scavenger-receptors (mal-BSA-Phthalocyanine). The abdominal aorta of Sprague-Dawley rat was injured by pulling an inflated balloon catheter. Photosensitizers (mal-BSA-Phthalocyanine, free Phthalocyanine) were injected 2 wk after surgery. Four hours following photosensitizers injection, (1) abdominal aorta retrieved and frozen tissue sections were examd. for arterial layer drug distribution using fluorescence microscopy. (2) **Photodynamic therapy** (**PDT**) was performed on abdominal artery by using argon dye laser and 2 wk after **PDT**, pathol. anal. of the arteries were performed by measuring the ratio of IH thickness (IH thickness / Media thickness). Mal-BSA-Pc fluorescence from fully-developed neointimal tissue (1446.4 a.u.) is higher than abdominal media (1063.4 a.u.) and adventitia (680.0 a.u.). In contrast, Pc dose not selectively accumulate in the intimal hyperplastic lesion, eg; intimal hyperplastic lesion (597.5 a.u.), media (872.7 a.u.), adventitia (847.5 a.u.). Mal-BSA-Pc ratio of IH thickness is significantly lower (43.1 .+-. 2.2%) than Pc (59.9 .+-. 3.8%), Laser irradn. only (76.6 .+-. 4.1%) and control (105.6 .+-. 5.9%) ($p<0.001$). We conclude that mols. can be selectively delivered to **intimal hyperplasia** via a receptor-mediated process.

L10 ANSWER 42 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:319963 HCAPLUS
DOCUMENT NUMBER: 126:327524
TITLE: Delivery of benzoporphyrin derivative, a photosensitizer, into atherosclerotic plaque of Watanabe heritable hyperlipidemic rabbits and balloon-injured New Zealand rabbits
AUTHOR(S): Allison, B. A.; Crespo, M. T.; Jain, A. K.; Richter, A. M.; Hsiang, Y. N.; Levy, J. G.
CORPORATE SOURCE: Department of Surgery, University of British Columbia, Vancouver, BC, V6T 2B5, Can.
SOURCE: Photochemistry and Photobiology (1997), 65(5), 877-883
CODEN: PHCBAP; ISSN: 0031-8655
PUBLISHER: American Society for Photobiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In this study we compared the plasma distribution and arterial accumulation of a photosensitizer, benzoporphyrin deriv. (BPD) monoacid ring A, in two models of atherosclerosis: the spontaneous lesions of the Watanabe heritable hyperlipidemic (WHHL) rabbit and induced lesions of the balloon-injured, cholesterol-fed New Zealand white (NZW) rabbit. Selective uptake and retention of a photosensitizer by the abnormal portion of a vessel is a necessity in order for **photodynamic therapy** to become a successful modality for inhibition of **intimal hyperplasia**, selective removal of atherosclerotic tissue or imaging of diseased arteries. Liposome-based formulations were compared to freshly isolated native low d. lipoprotein (LDL) and acetylated-LDL (Ac-LDL) as delivery vehicles for BPD. Plasma distribution of the photosensitizer was analyzed by KBr d. gradient ultracentrifugation. Although the delivery vehicle influenced plasma distribution immediately postinjection, BPD subsequently partitioned according to the plasma concn. of the lipoproteins. Photosensitizer level in plaque and normal artery specimens was detd. by Et acetate extn. and spectrofluorometric measurement. The measurement of BPD in normal and atherosclerotic arterial tissue demonstrated a selective accumulation in atherosclerotic tissue. Preassocn. with LDL and Ac-LDL enhanced accumulation of BPD in atherosclerotic tissue when compared with normal artery (mean ratios of 2.8 and 4.1 were achieved, resp.). These results indicate that the preferential uptake of BPD by atherosclerotic plaque can be enhanced by preassocn. with plasma lipoproteins, suggesting that light activation could lead to a highly selective destruction of diseased vascular tissue.

L10 ANSWER 43 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:189107 HCAPLUS
DOCUMENT NUMBER: 126:222370
TITLE: **Photodynamic therapy** of extracellular matrix stimulates endothelial cell growth by inactivation of matrix-associated transforming growth factor-.beta.
AUTHOR(S): Van Eps, Randolph G. Statius; Adili, Farzin; Watkins, Michael T.; Anderson, R. Rox; Lamuraglia, Glenn M.

CORPORATE SOURCE: Division of Vascular Surgery and Wellman Laboratories of Photomedicine, Harvard Medical School, Massachusetts General Hospital, Boston, MA, 02114, USA
SOURCE: Laboratory Investigation (1997), 76(2), 257-266
CODEN: LAINAW; ISSN: 0023-6837
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

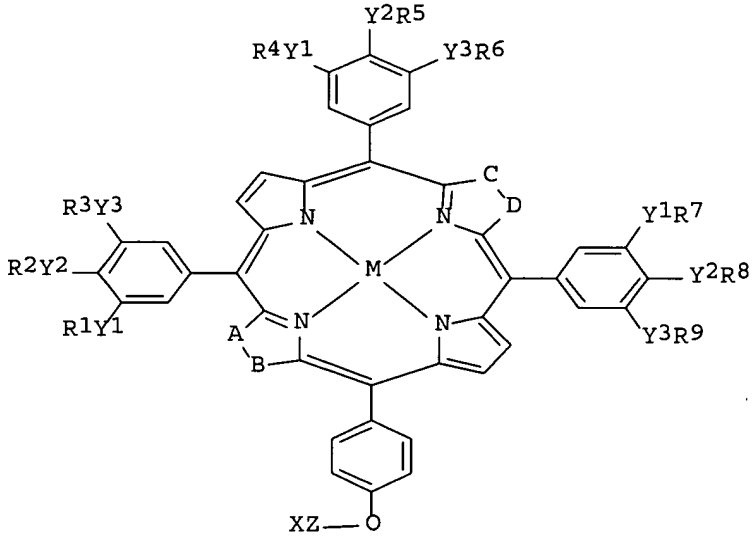
AB **Photodynamic therapy** (**PDT**), the prodn. of cytotoxic free-radical moieties by light activation of photosensitizer dyes, is a novel approach to inhibit exptl. **intimal hyperplasia**. Local eradication of vascular cells with this method in vivo is followed by expedient reendothelialization, and **PDT** of extracellular matrix (ECM) in vitro stimulates endothelial cell (EC) growth. This in vitro study explored one possible mechanism underlying these findings by investigating the effects of **PDT** on matrix-assocd. transforming growth factor-.beta. (TGF-.beta.), a potent inhibitor of EC growth. The ECM deposited by EC on tissue culture plates contained 85.4 .+-. 10.2 pg/10 cm2 of TGF-.beta., as measured by an ELISA. In contrast, after **PDT** of ECM, levels of TGF-.beta. could be barely be detected (0.2 .+-. 0.5 pg/10 cm2). The functional consequence of this observation was demonstrated by the finding that **PDT** of plates coated with a fibronectin-TGF-.beta. complex stimulated EC mitogenesis (102.3% .+-. 19.3%, $p < 0.0005$) compared with the untreated control (44.1% .+-. 13.5%). The inhibitory effect of ECM-assocd. TGF-.beta. on EC was further delineated by blocking its activity with a specific antibody. Whereas the antibody did not affect EC mitogenesis on **PDT**-treated matrix or matrix-free plates (101% .+-. 8.8%, 105.6% .+-. 9.8%), EC mitogenesis growing on ECM was significantly enhanced (125.9% .+-. 17.5%, $p < 0.05$). Finally, SDS-PAGE anal. of **PDT** -treated TGF-.beta. in soln. demonstrated that the **PDT**-mediated loss of TGF-.beta. activity was not assocd. with changes in its mol. wt. These data demonstrate that increased EC proliferation on **PDT** -treated matrix is, at least in part, mediated by inactivation of TGF-.beta.. **PDT**-removal of this EC growth inhibitor in the intima provides a mechanism by which **PDT** of the vascular wall could potentiate endothelial regrowth, a factor which may promote proper healing and result in the inhibition of **intimal hyperplasia**.

=> d ibib abs 30-35

L10 ANSWER 30 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:161288 HCAPLUS
DOCUMENT NUMBER: 132:202301
TITLE: Preparation of metalloporphyrin and porphyrin derivatives, their use in **photodynamic therapy** and medical devices containing them
INVENTOR(S): Love, William Guy; Cook, Michael John; Russell, David Andrew
PATENT ASSIGNEE(S): Destiny Pharma Limited, UK; University of East Anglia
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000012512	A1	20000309	WO 1999-GB2864	19990831
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2341507	AA	20000309	CA 1999-2341507	19990831
AU 9956360	A1	20000321	AU 1999-56360	19990831

EP 1107971 A1 20010620 EP 1999-943075 19990831
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2002523509 T2 20020730 JP 2000-567534 19990831
PRIORITY APPLN. INFO.: GB 1998-18789 A 19980828
GB 1999-12971 A 19990604
WO 1999-GB2864 W 19990831
OTHER SOURCE(S): MARPAT 132:202301
GI



I

AB Metalloporphyrins (I) are prepd., wherein R1, R2, R3, R4, R5, R6, R7, R8, R9 and X have meanings given in the description and Y1, Y2 and Y3 are either absent or represent O, Z is absent or represents lower alkylene, M is a metal or metalloid and A-B and C-D are independently CH:CH or CH2CH2, which are useful in the treatment of medical conditions for which a photodynamic compd. is indicated. Compns., app. and methods of treatment of a medical condition for which a photodynamic compd. is indicated are also disclosed. Thus, {5,5'-{4,4'-[12,12'-dithiobis(dodecyloxy)phenyl]}-10,10',15,15',20,20'-hexakis(3,4,5-tridecyloxyphenyl)diporphyrinato}zinc was prepd. and deposited on the surface of a gold coated vascular stent for use in **photodynamic therapy**.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 31 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:146608 HCAPLUS
DOCUMENT NUMBER: 132:276028
TITLE: **Photodynamic therapy** generates a matrix barrier to invasive vascular cell migration
AUTHOR(S): Overhaus, Marcus; Heckenkamp, Joerg; Kossodo, Sylvie; Leszczynski, Dariusz; LaMuraglia, Glenn M.
CORPORATE SOURCE: Division of Vascular Surgery and the Wellman Laboratories of Photomedicine, Harvard Medical School, Massachusetts General Hospital, Boston, MA, 02114, USA
SOURCE: Circulation Research (2000), 86(3), 334-340
CODEN: CIRUAL; ISSN: 0009-7330
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Photodynamic therapy** (**PDT**) inhibits exptl. **intimal hyperplasia**. **PDT** results in complete vascular wall cell eradication with subsequent adventitia but minimal media repopulation. This study was designed to test the hypothesis that

PDT alters the vascular wall matrix thereby inhibiting invasive cell migration, and as such, provides an important barrier mechanism to favorably alter the vascular injury response. Untreated smooth muscle cells (SMCs) and fibroblasts were seeded on control and **PDT** -treated (100 J/cm2; photosensitizer was chloroaluminum-sulfonated phthalocyanine, 5 .mu.g/mL) 3-dimensional collagen matrix gels. Invasive cell migration was temporally quantified by calibrated microscopy. Zymog. and ELISA assessed SMC matrix metalloproteinase levels. Mol. changes of gel proteins and their susceptibility to collagenase were analyzed by SDS-PAGE and Western blot. Limited pepsin digestion and histol. were used to assess the in vivo relevance of the model, using an established rat carotid artery model at 1 and 4 wk after balloon injury and **PDT**. **PDT** of 3-dimensional matrix of gels led to a 52% redn. of invasive SMCs and to a 59% redn. of fibroblast migration ($P<0.001$) but did not significantly affect secretion of matrix metalloproteinases. **PDT** induced collagen matrix changes, including crosslinking, which resulted in resistance to protease digestion. **PDT** led to a durable 45% redn. in pepsin digestion susceptibility of treated arteries ($P<0.001$) and inhibition of periadventitial cell migration into the media. These data suggest that **PDT** of matrix gels generates a barrier to invasive cellular migration. This newly identified effect on matrix proteins underscores its pleiotropic actions on the vessel wall, and as such, **PDT** may be of considerable potential therapeutic value to inhibit **restenosis**.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 32 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:81648 HCAPLUS
DOCUMENT NUMBER: 132:177485
TITLE: Reduction in the response to coronary and iliac artery injury with **photodynamic therapy** using 5-aminolevulinic acid
AUTHOR(S): Jenkins, Michael P.; Buonaccorsi, Giovanni A.; Mansfield, Richard; Bishop, Christopher C. R.; Bown, Stephen G.; McEwan, Jean R.
CORPORATE SOURCE: National Medical Laser Centre, Department of Surgery, Royal Free and University College Medical School, London, UK
SOURCE: Cardiovascular Research (2000), 45(2), 478-485
CODEN: CVREAU; ISSN: 0008-6363
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Photodynamic therapy** (**PDT**) uses red light (non-thermal, non-ionizing) to activate a previously administered photosensitizing drug. This inhibits neointimal hyperplasia in injured arteries in small animals where it appears safe and well tolerated. Our aim was to develop a method for percutaneous application of **PDT** to iliac and coronary arteries in a large animal model and investigate its influence on the remodeling and intimal hyperplastic response to balloon injury. Studies were undertaken on 13 juvenile Large White-Landrace crossbred pigs (15-20 kg). After i.v. administration of the photosensitizing agent 5-amino levulinic acid (ALA), the arterial tree was accessed via the left common carotid artery and balloon injuries made by overdistension in both common iliacs (thirteen animals) and one or two main coronary arteries (eight animals). Half the injured sites were then illuminated with red laser light transmitted via the catheter. Animals were culled 28 days later and tissue harvested for histomorphometry. Compared with control injured vessels, **PDT** treated, balloon-injured coronary arteries had a larger lumen (1.4 vs. 0.8 mm2, $P=0.002$), larger area within the external elastic lamina (2.8 vs. 2.2 mm2, $P=0.006$) and smaller area of neointimal hyperplasia (0.4 vs. 0.7 mm2, $P=0.06$), 28 days after intervention. Less neointimal hyperplasia and the absence of neg. remodeling resulted in the lumen of **PDT**-treated, injured segments being the same as that of adjacent ref. segments (1.5 vs. 1.6 mm2). Similar trends, but with smaller differences, were seen in the iliac vessels. Intra-arterial, trans-catheter **PDT** favorably influences the arterial response to balloon injury in both the coronary and peripheral circulations. This technique offers a promising new approach to **restenosis** after endovascular procedures.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 33 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:34766 HCAPLUS
DOCUMENT NUMBER: 132:73669
TITLE: Texaphyrins as co-therapeutic sensitizers for treatment of macrophage-mediated disease
INVENTOR(S): Woodburn, Kathryn W.; Young, Stuart W.
PATENT ASSIGNEE(S): Pharmacyclics, Inc., USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000001414	A1	20000113	WO 1999-US15199	19990706
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2336134	AA	20000113	CA 1999-2336134	19990706
AU 9948608	A1	20000124	AU 1999-48608	19990706
EP 1094840	A1	20010502	EP 1999-932263	19990706
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002519390	T2	20020702	JP 2000-557860	19990706
NO 2001000044	A	20010301	NO 2001-44	20010104
US 2002115649	A1	20020822	US 2001-755795	20010105

PRIORITY APPLN. INFO.: US 1998-110509 A 19980706
US 1998-155208P P 19980706
WO 1999-US15199 W 19990706

AB The invention provides methods for treating disease by sensitizing the effects of a co-therapeutic agent in macrophages. The method comprises administering a texaphyrin and a co-therapeutic agent. Texaphyrins are provided for enhancing the cytotoxicity of therapeutic agents in macrophage-mediated disease since texaphyrins have been shown to accumulate in macrophage.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 34 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:682214 HCAPLUS
DOCUMENT NUMBER: 132:10414
TITLE: Significance of dosimetry in **photodynamic therapy** of injured arteries: classification of biological responses
AUTHOR(S): Adili, Farzin; Van Eps, Randolph G. Statius; LaMuraglia, Glenn M.
CORPORATE SOURCE: Division of Vascular Surgery and the Wellman Laboratories of Photomedicine, Harvard Medical School, Massachusetts General Hospital, Boston, MA, 02114, USA
SOURCE: Photochemistry and Photobiology (1999), 70(4), 663-668
CODEN: PHCBAP; ISSN: 0031-8655
PUBLISHER: American Society for Photobiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB With conflicting results in the literature on the ability of **photodynamic therapy** (**PDT**) to inhibit **intimal hyperplasia** (IH), the present study systematically investigated the effects of drug and light dosimetry on the biol. responses in the artery wall. The rat common carotid artery was balloon-injured and pressurized with benzoporphyrin-deriv. monoacid ring (BPD). Then, **PDT** was performed with an external laser at different fluences and the biol. responses of the artery wall were histol. examd. at 24 h and at 2 wk. **Photodynamic therapy** effects on injured arteries can be classified into four stages: low-dose

PDT using 0.5 .mu.g/mL BPD at 50 J/cm2 (stage I) resulted in incomplete cell eradication and significant IH at 2 wk. Irradn. with 100 J/cm2 at the same BPD concn. (stage II) completely eradicated the cells in the artery wall at 24 h but still led to IH at 2 wk. However, 25 .mu.g/mL BPD at 100 J/cm2 (stage III) resulted in total cell eradication at 24 h and inhibition of IH at 2 wk. In contrast, high-dose **PDT** with 25 .mu.g/mL BPD and 200 J/cm2 (stage IV) led to thrombus development and vascular occlusion at 24 h. These data, demonstrating the different stages of **PDT** effects on injured arteries, emphasize the crit. importance of appropriate **PDT** dosimetry for the effective inhibition of IH.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 35 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:617856 HCAPLUS
DOCUMENT NUMBER: 132:119348
TITLE: Different effects of **photodynamic therapy** and .gamma.-irradiation on vascular smooth muscle cells and matrix: Implications for inhibiting **restenosis**
AUTHOR(S): Heckenkamp, Joerg; Leszczynski, Dariusz; Schiereck, Jan; Kung, Justin; LaMuraglia, Glenn M.
CORPORATE SOURCE: Division of Vascular Surgery of the General Surgical Services, Wellman, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 02114, USA
SOURCE: Arteriosclerosis, Thrombosis, and Vascular Biology (1999), 19(9), 2154-2161
CODEN: ATVBFA; ISSN: 1079-5642
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB .gamma.-Irradn. (.gamma.-RT) and **photodynamic therapy** (**PDT**) are known to inhibit **intimal hyperplasia**. The common mechanism is that both modalities produce free radicals, but unlike .gamma.-RT, **PDT** generates them through the absorption of light by photosensitizers. The purpose of this in vitro study was to assess the differences that **PDT** and .gamma.-RT have on the fibroproliferative response after vascular injury by comparing their effects on vascular smooth muscle cells (SMCs) and on the extracellular matrix (ECM). Mitochondrial activity (tetrazolium salt), proliferation ([3H]thymidine incorporation), and the mechanisms of cell death (terminal deoxynucleotidyl transferase-mediated dUTP biotin nick end labeling [TUNEL] staining) were used to assess differences between **PDT** (100 J/cm2) and .gamma.-RT (10 or 20 Gy) on SMC injury. The different effects on bioregulatory mols. were investigated by quantitating the proliferation of SMCs cultured with conditioned medium and on treated ECM. **PDT** of SMCs reduced proliferation and mitochondrial activity (0.5.+-.0.75% and 1.7.+-.4.25%, resp., P<0.0001), whereas .gamma.-RT of SMCs decreased cell proliferation but did not affect metabolic activity. Stimulation with calf serum of .gamma.-RT-treated SMCs did not affect proliferation but increased mitochondrial enzyme activity (160.+-.11%, P<0.0005). The conditioned medium, derived from **PDT**- but not .gamma.-RT-treated SMCs, did not stimulate effector SMC proliferation compared with .gamma.-RT-treated SMCs (16.+-.4.1% vs. 80.+-.16.8%, P<0.0001). Apoptosis was the principle cytotoxic mechanism after **PDT**, whereas .gamma.-RT cells were growth arrested but viable. **PDT** of the ECM reduced effector SMC proliferation compared with controls and .gamma.-RT cells (18.+-.6.5% vs. 100.+-.17.7% and 84.+-.8.9%, resp., P<0.0001). These data suggest that .gamma.-RT and **PDT** may inhibit **restenosis** but by different mechanisms. The effects of **PDT** are more diverse and may result in improved outcome while avoiding the teratogenic exposure due to ionizing irradn.
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs 36-39

L10 ANSWER 36 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:307336 HCAPLUS
DOCUMENT NUMBER: 131:113146
TITLE: Potential applications of **photodynamic**

therapy
AUTHOR(S): Okunaka, Tetsuya; Kato, Harubumi
CORPORATE SOURCE: Department of Surgery, Tokyo Medical University, Tokyo, 160-0023, Japan
SOURCE: Reviews in Contemporary Pharmacotherapy (1999), 10(1), 59-68
CODEN: RCPHFW; ISSN: 0954-8602
PUBLISHER: Marius Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with over 100 refs. At the present time, **photodynamic therapy** (**PDT**) is under active investigation for a range of therapeutic applications, in both oncol. and nononcol. areas of medicine. In oncol., a no. of studies have indicated that **PDT** has potential in the laser treatment of malignant tumors. In addn., **PDT** may be used preoperatively to increase operability, and reduce the extent of required resection, in the surgical treatment of lung cancer. The results of preclin. investigations have suggested that **PDT** may be useful in bone marrow purging to eliminate malignant cells prior to marrow transplantation, and clin. trials are now underway to examine this further. A particularly successful use of **PDT** is likely to be for the treatment of Barrett's oesophagus where malignancy may involve long sections of oesophagus, with multifocal and unpredictable distribution. A no. of nononcol. applications for **PDT** have been proposed. For example, initial studies suggest that it may reduce nonchoroidal neovascularization in ocular vascular disease. **PDT** has also been investigated for use in treating atherosclerotic cardiovascular lesions or to prevent **restenosis** following balloon angioplasty, again with encouraging results. Under certain conditions, **PDT** may modulate immunol. processes, as a result of the destruction of immunol. active cells; it has been proposed that this property could be utilized to relieve rheumatic symptoms by down-regulating the cellular immune response in rheumatoid arthritis. Selective destruction of pathol. synovium, while leaving articular surfaces undamaged, may also be achieved by appropriate use of **PDT** . **PDT** may have some applications in virol.; its uses against papilloma virus and against HIV and blood-borne viruses are still under investigation. The accessibility of skin to light offers an opportunity for the use of **PDT** in the treatment of dermatol. conditions; early studies suggest that it can be helpful in psoriasis, while its uses in acne, alopecia areata, portwine stains and hair removal are also being investigated. The next few years will certainly see an expansion of the indications for **PDT**.

REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 37 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:765867 HCAPLUS
DOCUMENT NUMBER: 130:179366
TITLE: Low dose psoralen and UVA (PUVA) therapy enhanced arterial shrinkage after balloon angioplasty in rabbits
AUTHOR(S): Perree, Jop; Van Leeuwen, Ton G.; Velema, Evelyn; Borst, Cornelius
CORPORATE SOURCE: Department of Cardiology, Heart-Lung institute, Utrecht University Hospital, Utrecht, Neth.
SOURCE: Proceedings of SPIE-The International Society for Optical Engineering (1998), 3245(Lasers in Surgery: Advanced Characterization, Therapeutics, and Systems VIII, 1998), 44-50
CODEN: PSISDG; ISSN: 0277-786X
PUBLISHER: SPIE-The International Society for Optical Engineering
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Restenosis** after balloon angioplasty is caused by both **intimal hyperplasia** and arterial shrinkage (constrictive remodeling). Previous studies have indicated the inhibitory effect of **photodynamic therapy** on **intimal hyperplasia** development after angioplasty. The potential of a photoactivation regime (Psoralen + UVA irradn.: PUVA), which does not cause unwanted systemic side effects, for the prevention of both **intimal hyperplasia** formation and constrictive remodeling following balloon dilation was explored in the present study.

In the rabbit iliac artery, balloon dilation followed by PUVA-therapy at a radiant exposure of 1 J/cm2 was performed (n=10). Control balloon dilation was performed in the contralateral arteries (n=10). After 4 wk of survival, angiog. lumen renarrowing was detd. in terms of **intimal hyperplasia** and constrictive remodeling. Late loss, but not **intimal hyperplasia**, was significantly larger in the PUVA group as compared to the control group ($p<0.05$). This difference in angiog. lumen loss can only be attributed to the difference in constrictive remodeling (arterial shrinkage). Thus, PUVA-therapy did not prevent **intimal hyperplasia** following balloon dilation. PUVA-therapy even enhanced luminal narrowing by augmented constrictive arterial remodeling.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 38 OF 58 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:765865 HCAPLUS
DOCUMENT NUMBER: 130:179364
TITLE: Pharmacokinetics and efficacy of 5-aminolevulinic acid for endovascular **photodynamic therapy** in a swine model
AUTHOR(S): Jenkins, Michael P.; Buonaccorsi, Giovanni; MacRobert, Alexander; Bishop, Christopher C. R.; Bown, Stephen G.; McEwan, Jean R.
CORPORATE SOURCE: Department of Surgery, University College London, London, UK
SOURCE: Proceedings of SPIE-The International Society for Optical Engineering (1998), 3245(Lasers in Surgery: Advanced Characterization, Therapeutics, and Systems VIII, 1998), 20-27
CODEN: PSISDG; ISSN: 0277-786X
PUBLISHER: SPIE-The International Society for Optical Engineering
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Vascular smooth muscle cells (VSMC) are known to be important in **restenosis** and **photodynamic therapy** (**PDT**) has been shown exptl. to deplete the VSMC population in small animal studies. We aimed to investigate the pharmacokinetics of 5-aminolaevulinic acid (5-ALA) and to see if endovascular **PDT** was feasible in a large animal model. Large White pigs (15-20Kg) were photosensitized with 5-ALA at a concn. of 60 and 120 mg/Kg. Arterial biopsies were taken at intervals between 30 mins and 24 h and snap frozen in liq. nitrogen. Frozen sections were analyzed using a CCD camera and PpIX activity assessed by computing pixel counts for intima, media and adventitia at each time point. Based on the above results 8 pigs were treated with **PDT** at 1.5, 2.5 or 6 h following 5-ALA administration. Iliac segments were then illuminated with 50J/cm2, 635nm wavelength light via a 4mm transparent PTA balloon. Animals were culled at 3 days and the above segments pressure perfused in situ with 4% formyl saline, before being excised and fixed. Fluorescence peaked in the adventitia at 1.5 h, was minimal at 2.5 h and peaked in the media at 6 h post 5-ALA. Of the second series of 8 pigs, all animals survived to culling and all treated arteries remained patent. Histol. sections stained with H&E were examd. and medial VSMC's counted in 4 individual high power fields per section. The mean VSMC count per HPF for **PDT** treated segments was 16, 51 and 12 at 1.5, 2.5 and 6 h resp. VSMC counts in ALA alone controls and light alone controls were 115 and 103 resp. ($p<0.0001$). Endovascular delivery of light to 5-ALA sensitized animals is therefore feasible and was not assocd. with any complications.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 39 OF 58 HCAPLUS COPYRIGHT 2003 ACS
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TITLE: Importance of the treatment field for the application of vascular **photodynamic therapy** to inhibit **intimal hyperplasia**
AUTHOR(S): van Eps, Randolph G. Statius; ChandraSekar, N. R.; Hasan, Tayyaba; Lamuraglia, Glenn M.
CORPORATE SOURCE: Division of Vascular Surgery of the General Surgical Services, Wellman Laboratories of Photomedicine, MA, USA

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AB **Intimal hyperplasia** (IH) plays a dominant role in the development of **restenosis**. In previous studies, **photodynamic therapy** (**PDT**) prevented IH induced by segmental balloon injury of the rat carotid. The crit. elements required to control IH effectively with this technique are not fully understood. This study assessed the importance of the treatment field by studying the repair process of injured vessels, in which the **PDT**-treatment field did not target the entire injured area. The entire rat common carotid artery was balloon-injured to induce IH, whereas only the cervical segment below the bifurcation was subjected to **PDT** by external light irradn. after administration of the photosensitizer chloroaluminum sulfonated phthalocyanine. Light irradn. of injured arteries without photosensitizer served as control for **PDT**, and **PDT** of uninjured arteries was included as a control group for the balloon injury. Histol. characterization of the repair process was sequentially assessed. Balloon-injured arteries without **PDT** displayed rapid IH development with a peak at 2 wk. **Photodynamic therapy** of balloon-injured arteries resulted in complete local depletion of medial smooth muscle cells (SMC), which was assocd. with a lack of IH until 2 wk. However, at 4 and 16 wk there was significant IH in **PDT**-treated arteries despite a lack of medial SMC repopulation. A wave of IH progression over the acellular media was obsd. in these arteries, migrating from the injured non-**PDT**-treated area. The **PDT** of uninjured arteries did not result in IH and was also assocd. with a persistent acellular media. Delayed IH development after **PDT** of injured vessels can result from IH progression from an injured site not included in the treatment field. This also indicated that the source of cells developing the **intimal hyperplasia** lesion can originate from an area remote from the lesion. Together with previous results and the detn. that **PDT** itself does not induce IH, it can be reasoned that inclusion of the whole injured artery or a section of an uninjured margin in the treatment field is essential for effective **PDT** prevention of IH.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT